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09/403,967	03/28/2000	Bruno Guy	50019/006001	7903

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No. 09/403,967	Applicant(s) Guy et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 22, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *29-58* is/are pending in the application.

4a) Of the above, claim(s) *29-38, 40-42, 45, and 58* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39, 43, 44, and 49-57* is/are rejected.

7) ☒ Claim(s) *46-48* is/are objected to.

8) ☒ Claims *29-58* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 29-58 are pending.

Claims 39 and 46 have been amended.

Claims 29-38,40-42, 45 and 58 are withdrawn.

Claims 39, 43-44, 46-57 are under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

2. Claims 46-48 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Rejections/Objections Withdrawn

3. The title "Brief Description of the Drawings" has been inserted.

4. Claim 39 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment obviating the lack of antecedent basis for the word "composition".

5. Claims 46-48 rejected under 35 U.S.C. 112, second paragraph, for reciting the phrase "wherein the T helper 1-type immune response is measured in mice" in light of the amendment of claim 46 adding clarity to the claim from which claims 47 and 48 depend.

Rejections Maintained

6. The phrase "Abstract of the Disclosure" was not entered as only claims are recited on page 49 of the specification. An abstract on a separate page could obviate this objection. The last page of the specification is page 51. An abstract should be inserted at page 52.

7. Claims 39, 50-51 and 57 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,9-11,26 of U.S. Patent No. 6,126,938.

8. Claims 39, 44, 49-57 rejected under 35 U.S.C. 102(e) as being anticipated by Guy et al (US Pat. 6,126,938, different inventive entity).

9. Claims 39 and 43 rejected under 35 U.S.C. 103(a) as being unpatentable over Guy et al, as applied to claims 39, 44, 49-57 above, in view of Epand et al (US Pat. 5,283,185).

10. Claims 39 and 43 rejected under 35 U.S.C. 103(a) as being unpatentable over Guy et al, as applied to claims 39, 44, 49-57 above, in view of Lockhoff et al (US Pat. 4,855,283).

Response to Arguments

11. Applicant's arguments filed October 17, 2002 have been fully considered but they are not persuasive.

12. The rejection of claims 39, 50-51 and 57 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,9-11,26 of U.S. Patent No. 6,126,938 is traversed on the grounds that the "The methods of the claims of the present application, for example, require the use of particular lipids, saponins or lycolipopeptides" and

asserts that the "methods of the cited claims of '938 patent, in contrast, do not require the use of such an agent."

13. It is the position of the examiner that the "agent" of the instantly claimed invention are agents "derived from Helicobacter (instant claim 39, line 3)" and saponin is not derived from Helicobacter. The agents of the instantly claimed invention as defined in the instant specification are proteins, peptides, plasmids and DNA molecules of Helicobacter. Clearly the agents of the instant claims are generic claimed relative to the agents recited in the allowed claims of '938. The compounds of the instant method are adjuvants known in the art, and the combination of the agent and compound define the essential components of what is administered to a patient. The novelty of allowed claims in US Pat. 6,126,938, was the combination of agents, and how they were administered, ie DC-chol liposomes containing a plasmid encoding a Helicobacter agent. The elected invention directed to a cationic lipid is the defined carrier for the liposome/plasmid Helicobacter agent of '938, but the instantly claimed invention only comprises a single methods step to generically claim a method of inducing an immune response, while the allowed claims define a species of invention, claimed based upon a three step method to achieve the recited intended use of the method "to induce an immune response."

A comparison of the component parts of each method are set forth below, and was used in determining the basis for the obvious type double patenting rejection made of record in paper number 13.

Instant Application	Guy et al ' 938
Method of inducing an immune response	Method of inducing an immune response
TH-1	TH-1 (IgG2a, see figures 2B, 3A, 4A)
H.pylori agent (generically claimed includes plasmids, page 19, lines 9-27)	H.pylori agent (species)(plasmid (see col. 17, lines 22-30; and claims 3, 6-8, 9-11, 26, 13, 15)
cationic lipid (generic:definition includes DC-chol liposome, page 20, line 30)	cationic lipid (species)(DC-Chol liposome (col. 9, see lines 22-46)
Administering (generically recited) (defined to include a single or multiple steps)	Administering (species) (defined to be multiple steps (see claims)) see page 18, lines 1-9 and page 23, lines 20-38 and page 24, lines 1-8)

In the instantly claimed invention, liposomes are permitted when the agent induces a TH-1 immune response and is together with the cationic lipid which also will induce a T helper 1-type immune response: specific claim limitations recited in claim 39 "wherein said lipid is not provided in the form of a liposome when administered in the absence of any additional compounds that promotes the induction of a T-helper 1-type immune response against Helicobacter"

Raz et al (PNAS, May 1996) teaches that plasmid encoded antigens primarily induce a TH-I immune response (see abstract, and entire document).

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14. The rejection of claims 39, 44, 49-57 rejected under 35 U.S.C. 102(e) as being anticipated by Guy et al (US Pat. 6,126,938, different inventive entity) is traversed on the grounds that claim 39 recites that the cationic lipid " is not in the form of a liposome".

15. It is the position of the examiner that the exact claim limitations recited in claim 39 permit the use of liposomes when the agent contained in the liposomes induces a TH-1 immune response. The claim limitations are:

"wherein said lipid is not provided in the form of a liposome when administered in the absence of any additional compounds that promotes induction of a T helper 1-type immune response against Helicobacter"

Clearly, the newly added claim limitations set forth a double negative. The first negative being "not provided" and the second being "in the absence". The combination of these two phrases permit the utilization of liposomes only when "additional compounds" are present that "promotes induction of a T helper 1-type immune response against Helicobacter." Guy et al show the cationic lipid liposomes to comprise a Helicobacter encoding agent plasmid that induced a TH-1 immune response (IgG2a). Plasmid encoding agents are known to induce a TH-I immune response (see Raz et al, 1996, PNAS, reference being made of record herein). Thus Guy et al, '938, anticipates the instantly claimed invention that includes the newly amended claim limitations.

16. The rejection of claims 39 and 43 under 35 U.S.C. 103(a) as being unpatentable over Guy et al, as applied to claims 39, 44, 49-57 above, in view of Epand et al (US Pat. 5,283,185), is

traversed on the grounds that "DC-chol used in the '938 patent is in the form of liposomes, which is excluded from the present claims when the method involves the administration of an immunogenic agent from Helicobacter and a cationic lipid, in the absence of any other Th-1 inducing agents.

17. It is the position of the examiner that the immunogenic agent of Guy et al '938, in plasmid form, is a TH-1 inducing agent, and the combination of the DC-chol liposome, the plasmid (TH-1 inducing agent) and the Helicobacter coding sequence (agent) meets the recited claim limitations.

While Guy et al '938 does not teach or suggest the utilization of DC-chol in a dispersion form, Epand et al (see col. 14, claim 1) provides motivation, and guidance through teaching DC-chol/nucleic acid agent dispersions to facilitate the transfer of DNA into mammalian cells (see col. 1, lines 1-8), has weak protein kinase C inhibitory activity (see col. 2, lines 68), and is a stable composition (see col. 3, lines 1-6 and Example XXVI) when used in a method that transfers nucleic acid molecules into mammalian cells. Guy et al teaches the utilization and stimulation of an immune response utilizing a DNA encoded agent together with a cationic lipid in association with the agent in vivo, and Epand shows a cationic lipid in association with a DNA encoded agent in a dispersion formulation for obtaining a stable composition, for the same purpose of transferring the nucleic acids into mammalian cells, the composition of Guy et al for induction of an immune response in a immunocompetent host.

Entry into a mammalian cell with a heterologous nucleic acid is a key step in the method of inducing an immune response and Epand et al teaches a method which defines through

utilization of a dispersion, an agent together with cationic lipid, this process is facilitated and will function both in vitro and in vivo (see col. 2, lines 33-42). Epand et al address disadvantages of methods known in the art that limit steps to be carried out in vitro, but teach a solution for in vivo utilization of the improved method that does not require a series of steps that prevent in vivo application of the method (see col. 2, lines 30-42). While Epand et al does not show in vivo administration of a composition, the reference does not teach away from in vivo administration of the cationic lipid/nucleic acid dispersion, and seeks to define more stable compositions that will function for nucleic acid transfer in vivo.

The rejection is maintained for reasons of record.

18. The rejection of claims 39 and 43 under 35 U.S.C. 103(a) as being unpatentable over Guy et al, as applied to claims 39, 44, 49-57 above, in view of Lockhoff et al (US Pat. 4,855,283) is traversed on the grounds that Lockhoff et al (US Pat. 4,855,283) does not provide any information as to what type of T-helper immune responses are induced.

19. It is the position of the examiner that Formula (I) is a second species of invention (iii) and was not intended to be considered a cationic lipid, analogous to DC-chol. The basis of the obviousness rejection was formulation of a bacterial agent (antigen) into a dispersion for administration. Guy et al teaches bacterial agent (antigen compositions) formulations that are not in dispersion form. Lockhoff et al was applied to the claims for teaching compositions for induction of "an increase in antibody synthesis" and evidence mitogenic properties (see col. 15,

lines 14-22) that are dispersions for stimulation of immune responses to bacterial agents. Additionally Lockhoff et al teach the compositions to "bring about an increase in the state of macrophages in vitro and in vivo" (see Lockhoff et al, col. 15, lines 14-27). Macrophage activation is associated with TH-1 immune responses and antibody production is associated with TH-2 immune responses. While the phrase "T-helper 1-type cell mediated immune response" is not recited in patent '283, the document clearly teaches through the utilization of agent/dispersion compositions in vivo results in an increase of macrophage activity (see Table 2, and col. 15, lines 14-55). The immune response induced is directed against the bacterial agent associated with the compound, the dispersion (solution,suspension) comprising a compound that functions as a mitogen, enhances stimulation of antibodies (a Th-1 immune response; see Lockhoff et al, col. 15, line 21), as well as stimulates an enhanced immune response directed to the immunogenic agent administered in association with the compound.

In the absence of a showing of unexpected results, Guy et al in view of Lockhoff et al, obviates the now claimed invention for reasons of record.

Conclusion

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp January 13, 2003

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